

FIG. 3

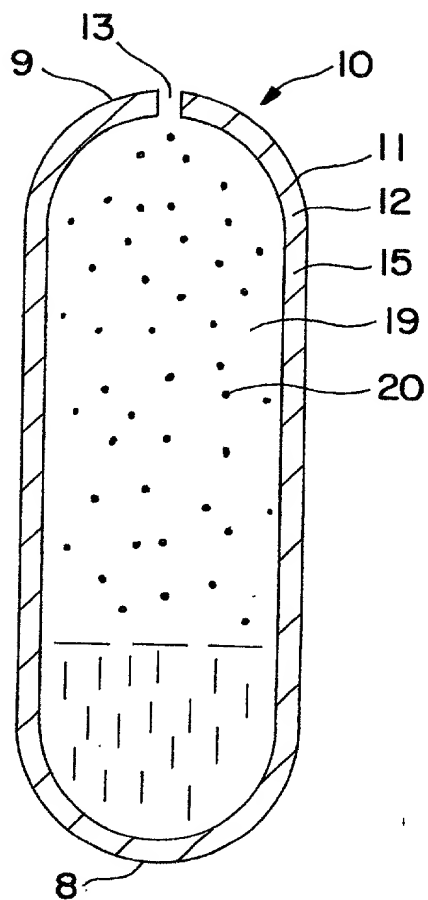


FIG. 4

A bar chart illustrating the release rate of 100 mg of 1% w/v hydrocortisone acetate over a 14-hour period. The y-axis represents the release rate in mg/hr, ranging from 0.00 to 50.00. The x-axis represents time in hours, ranging from 0.00 to 14.00. The release rate starts at approximately 20 mg/hr at 0 hours and decreases steadily to about 5 mg/hr at 14 hours. Error bars are included for each measurement.

Time (Hours)	Release Rate (mg/hr)
0.00	20.00
1.00	25.00
2.00	26.00
3.00	24.00
4.00	23.00
5.00	22.00
6.00	21.00
7.00	20.00
8.00	18.00
9.00	15.00
10.00	12.00
11.00	10.00
12.00	8.00
13.00	6.00
14.00	5.00

Figure 1 is a line graph showing the cumulative amount of dose (%) versus time (hours) for the release of 100 mg of 10% w/v polyvinyl alcohol solution from a 10% w/v polyvinyl alcohol solution. The y-axis is labeled 'CUMULATIVE AMOUNT OF DOSE (%)' and ranges from 0.00 to 100.00. The x-axis is labeled 'TIME (HOURS)' and ranges from 0.00 to 14.00. The graph shows a linear increase in cumulative dose over time, reaching approximately 95% at 14 hours. Error bars are included for each data point.

Time (Hours)	Cumulative Amount of Dose (%)
0.00	0.00
0.50	2.00
1.00	4.00
1.50	6.00
2.00	8.00
2.50	10.00
3.00	12.00
3.50	14.00
4.00	16.00
4.50	18.00
5.00	20.00
5.50	22.00
6.00	24.00
6.50	26.00
7.00	28.00
7.50	30.00
8.00	32.00
8.50	34.00
9.00	36.00
9.50	38.00
10.00	40.00
10.50	42.00
11.00	44.00
11.50	46.00
12.00	48.00
12.50	50.00
13.00	52.00
13.50	54.00
14.00	56.00

FIG. 5B

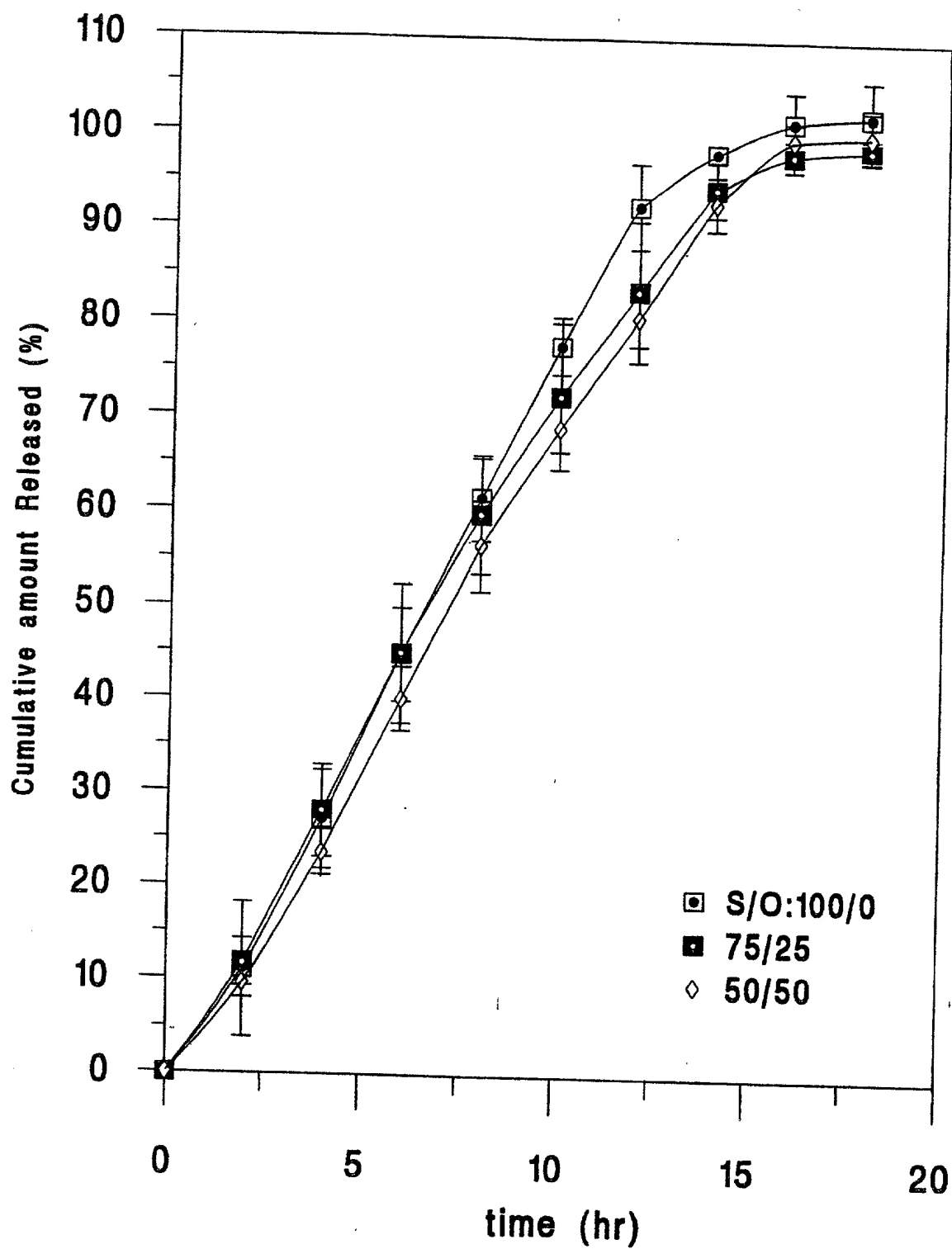
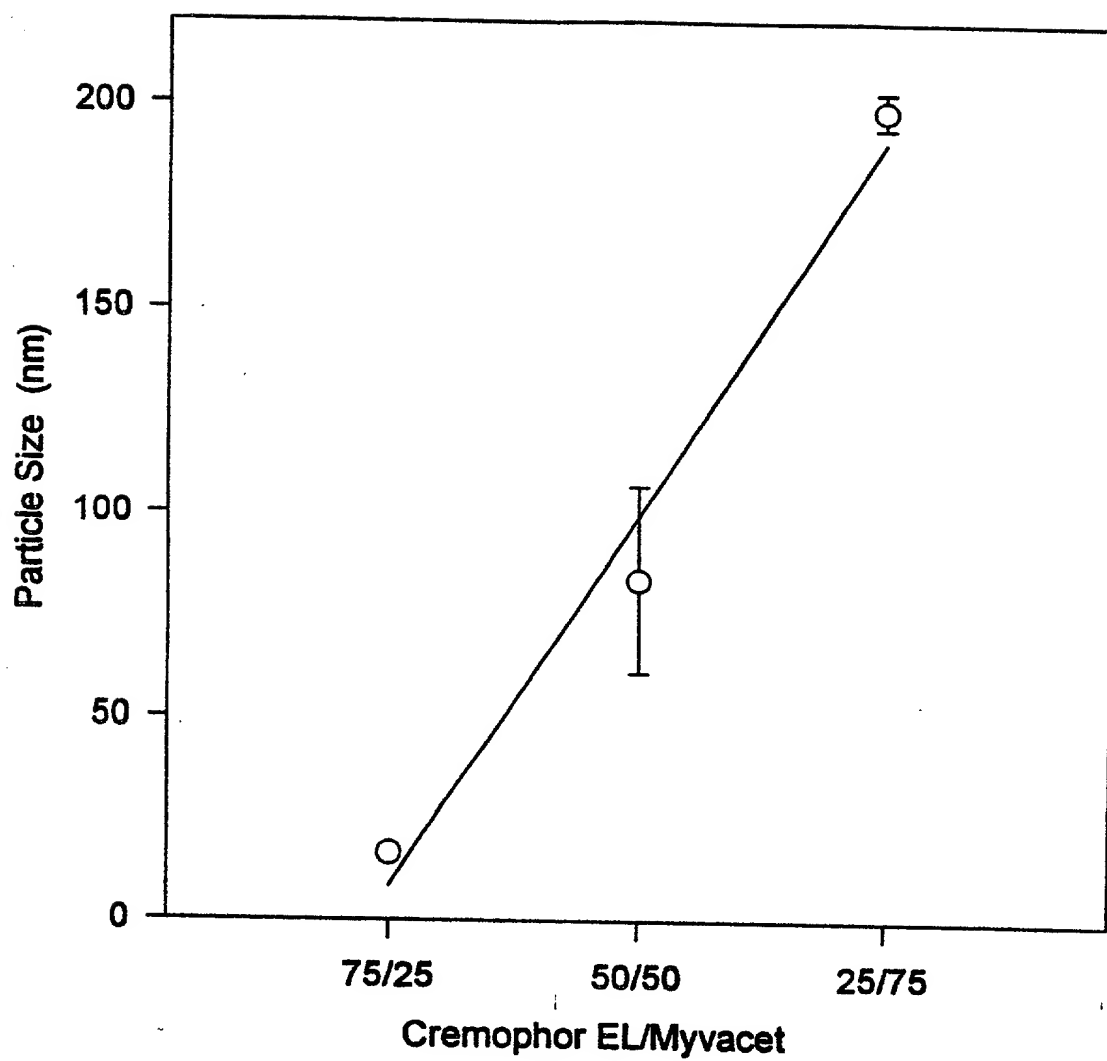


FIG. 6

A ternary phase diagram for the EL/Myvacet/Water system. The vertices represent 100% of each component: Water at the top, EL (Cremophor EL) at the bottom-left, and Myvacet at the bottom-right. The diagram is divided into two regions by a boundary line: 'EL/Myvacet 25/75' above and 'Microemulsion' below. The boundary line starts at approximately 25% EL and 75% Myvacet, curves towards the Water vertex, and then curves back towards the EL-Myvacet base. Data points are plotted as open circles, solid circles, open triangles, and solid triangles. The axes are marked with percentages: Water (0 to 100), EL (0 to 100), and Myvacet (0 to 100). Specific points on the boundary are labeled '50/50' and '75/25'.

## Cremophor EL

FIG. 7



**FIG. 8**



A line graph showing the relationship between progesterone solubility and liquid carrier concentration in water. The y-axis is labeled 'progesterone solubility (mg/ml)' and ranges from 0.0 to 1.5. The x-axis is labeled 'Liquid Carrier Concentration in Water (mg/ml)' and ranges from 0 to 25. The graph shows a curve starting at (0, 0) and increasing as the carrier concentration increases. Data points are plotted at 0, 5, 10, and 20 mg/ml carrier concentration, with two points each at 5, 10, and 20 mg/ml. The solubility increases from 0.0 mg/ml at 0 mg/ml carrier concentration to approximately 1.3 mg/ml at 20 mg/ml carrier concentration.

Liquid Carrier Concentration in Water (mg/ml)	progesterone solubility (mg/ml)
0	0.0
5	0.35
5	0.40
10	0.80
10	0.82
20	1.28
20	1.30

FIG. 10



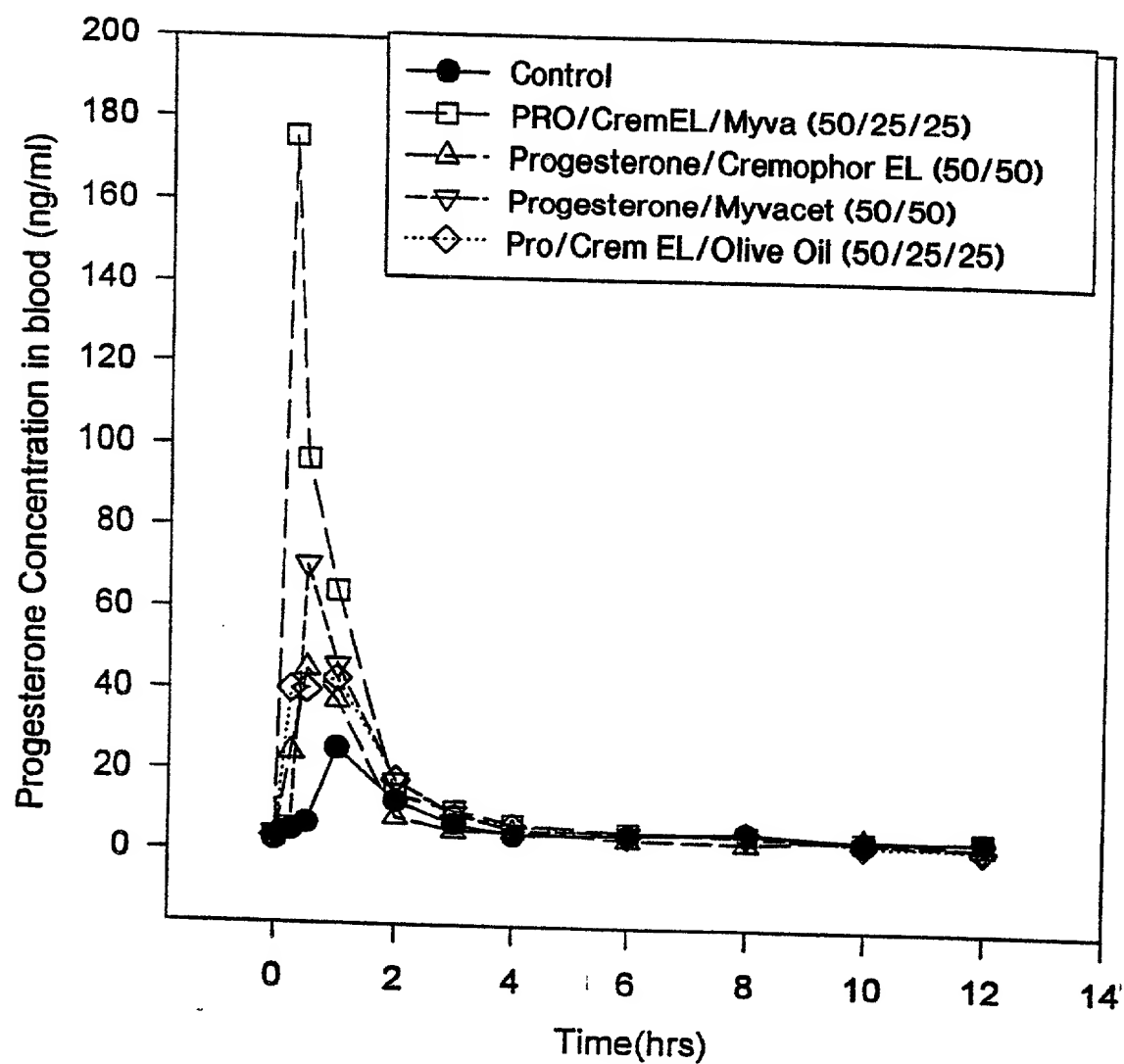


FIG. II

Figure 1 is a line graph showing the Progesterone Concentration in Blood Serum (ng/ml) versus Time (hrs) for three dogs (dog 1, dog 2, dog 3) at three different time points (0, 1, and 2 hours). The y-axis ranges from 0 to 300 ng/ml, and the x-axis ranges from 0 to 14 hours. The graph shows a sharp increase in progesterone concentration at 1 hour for all three dogs, peaking around 250 ng/ml for dog 1, 150 ng/ml for dog 2, and 100 ng/ml for dog 3. The concentration then decreases rapidly, returning to near baseline levels by 2 hours and remaining stable thereafter.

Time (hrs)	in dog 1 (●)	in dog 2 (■)	in dog 3 (▲)	in dog 1 (○)	in dog 2 (□)	in dog 3 (△)
0	~5	~5	~5	~5	~5	~5
1	~250	~150	~100	~250	~150	~100
2	~10	~10	~10	~10	~10	~10
4	~5	~5	~5	~5	~5	~5
6	~5	~5	~5	~5	~5	~5
8	~5	~5	~5	~5	~5	~5
10	~5	~5	~5	~5	~5	~5
12	~5	~5	~5	~5	~5	~5

FIG. 12

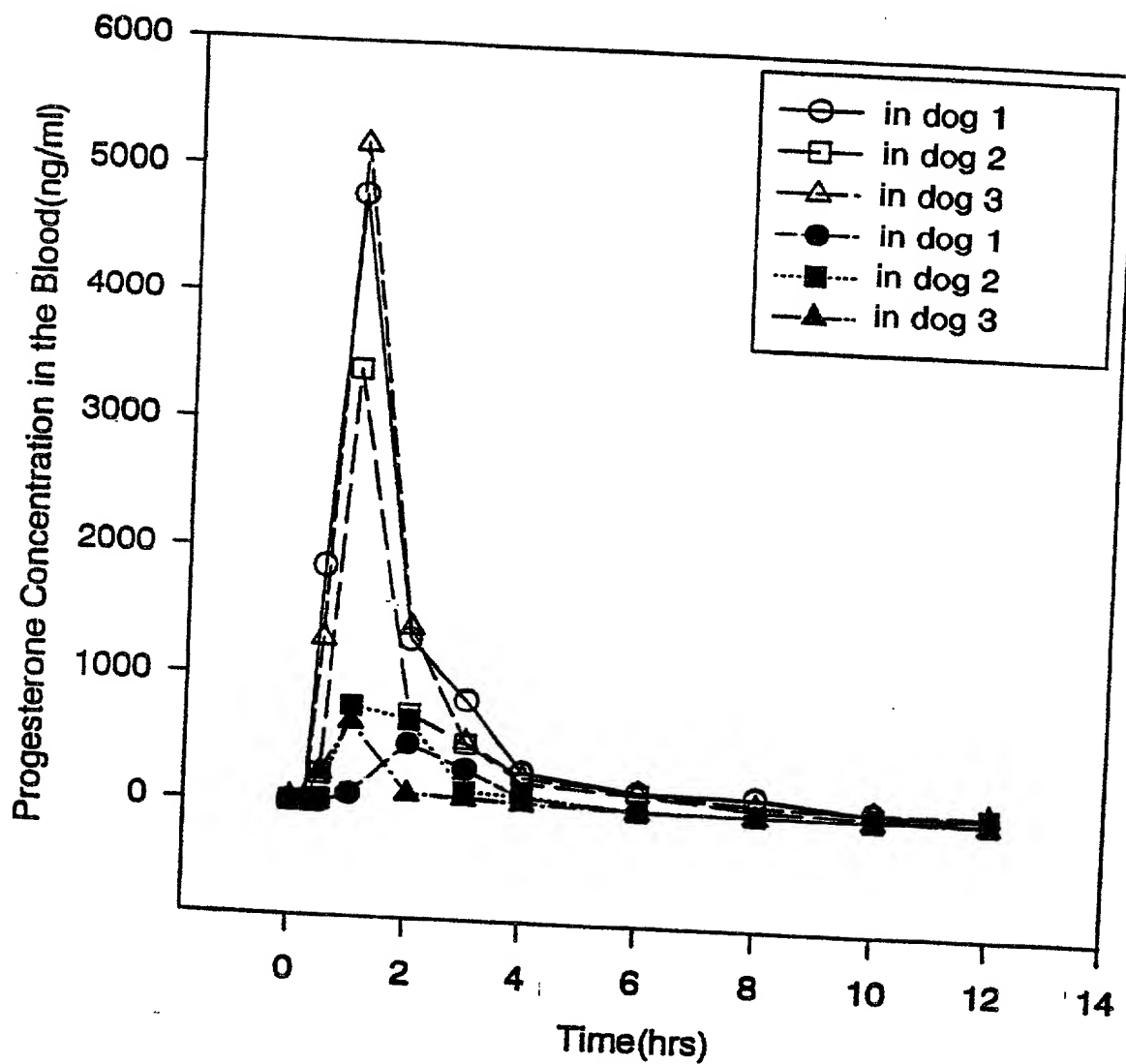


FIG. 13

**Pharmacokinetic Data for Oral Progesterone  
Formulations Dosed to Dogs (40mg)**

Formulation #	T <sub>max</sub> (h)				C <sub>max</sub> (ng/ml)				AUC (ng/ml*h)		*Relative BA % Average (s.d)	
	Dog 1	2	3	Avg	Dog 1	2	3	Avg (s.d).				
1	1	1	1	1	38.4	13.9	24.4	25.6(12.3)	104	51	104	100
2	0.25	0.50	0.25	0.33	252	90.8	248	197(92)	226	113	265	232 (21)
3	0.50	0.25	0.50	0.42	53.4	57.7	33.7	48.3(12.8)	109	95	102	130 (50)
4	0.5	1	1	0.83	174	57.1	30.4	87.2(76.4)	167	289	73	176(108)
5	0.5	1	0.25	0.58	57.2	70.8	74.7	67.5(9.1)	114	342	86	181(141)

AUC is calculated by trapezoidal rule from time zero to the last blood sampling point (12h).

The relative bioavailability is the ratio of AUC for liquid formulations to that for laqueus drug-layer formulation.

**Formulation Composition (wt%)**

Components	Formulation #				
	1	2	3	4	5
Progesterone	60	4	4	4	4
Mannitol	21				
Ac-di-sol	10				
Myji 52-s	5				
HPMC E-5	3				
Mg stearate	1				
Cremophor EL		48	96		48
Myvacet 9-45		48			
Olive oil				96	48

**FIG. 14**

**Pharmacokinetic Data for Emulsion Progesterone Formulation and  
Nonemulsion Push-Pill Drug-Layer Formulation (300mg dose)**

Formulation #	T <sub>max</sub> (h)				C <sub>max</sub> (ng/ml)			AUC (ng/ml*h)				Relative BA (%) Average (s.d)	
	Dog 1	2	3	Avg	Dog 1	2	3	Avg (s.d).	Dog 1	2	3		Avg.(s.d)
Nonemulsion	2	1	1	1.33	489	778	649	639(145)	1101	1715	898	1238(425)	100
Emulsion	1	1	1	1	4800	3420	5180	4467(926)	7715	4708	7418	6614(1657)	600 (289)

AUC is calculated by trapezoidal rule from time zero to the last blood sampling point (12h).  
The relative bioavailability is the ratio of AUC for liquid formulations to that for MPA-22 drug-layer formulation.

**Formulation Composition (wt%)**

Components	Nonemulsion Drug-Layer	Emulsion Oral Formulation
Progesterone	60	50
Mannitol	21	
Ac-di-sol	10	
Myji 52-s	5	12.5
HPMC E-5	3	
Mg stearate	1	
Cremophor EL		25.0
Myvacet 9-45		12.5

**FIG. 15**